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10/660,434	09/10/2003	Guennadi V. Glinskii	23543-07570	4883

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EXAMINER

LIN, JERRY

ART UNIT	PAPER NUMBER
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1631

MAIL DATE	DELIVERY MODE
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02/06/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,434	GLINSKII, GUENNADI V.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 and 36-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 36-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 14, 2007 has been entered.

Election/Restrictions

2. The Applicant's election with traverse of Table 69 in the reply filed on November 21, 2001 is acknowledged. The traversal is on the ground(s) that there would be no increased search burden to search a table in its entirety as compared to 60%-100% of a table. The Examiner agrees and withdrawn to requirement to elect a particular percentage of gene in a table and the genes that comprise that percentage. However, the restriction regarding an election of a Table is maintained, because each table of genes represents an independent and distinct invention and a search of all the Tables would be an undue burden.

It is noted that the Applicant had initially elected Table 5 in a previous restriction requirement. However, because the Examiner never searched the prior art Table 5, the Examiner will accept the Applicant's election of Table 69 and withdraw Table 5.

The requirement is made FINAL.

Status of the Claims

Claims 1-28 and 36-38 are under examination.

Regarding claims 24-28, the Table 69 was elected as species, and the other tables are withdrawn as being drawn to a non-elected species.

Specification

3. The use of the trademarks GENBANK, AFFYMETRIX MICRODB, AFFYMETRIX DMT, etc. has been noted in this application. Trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Please capitalize all trademarks.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24-28 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Instant claims 24-28 and 36-38 refer to Table 69. However, Table 69 has been amended to recite that the listed genes correspond to SEQ ID Nos 2240-2265. A Sequence Listing with SEQ ID Nos. 2240-2265 was filed after the First Office Action. However, SEQ ID Nos 2240-2265 (25 Seq ID Nos) do not correspond to the listed genes in table 69, because there are only 14 listed genes. Furthermore, the Examiner searched GenBank for the listed GenBank IDs listed in Table 69, but the GenBank IDs do not appear to exist. Thus, the Sequences Nos listed in the sequence listing cannot be correlated with the GenBank IDs. Because the sequence listing was not submitted with the originally filed disclosure and the sequences do not correspond to the genes listed in Table 69, the listed sequences are NEW MATTER.

Claim Rejections - 35 USC § 112, 2nd

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-28 and 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 24-28 and 36-38 are unclear because the GenBank IDs in the tables do not exist and the Sequence Nos do not correspond to the number of genes in the table. Table 69 lists GenBank ID, LocusLink Name, Gene Name and a UniGene ID. However,

upon searching GenBank, the listed GenBank IDs do not appear to exist. Additionally, the Seq ID Nos listed at the top of the table do not correspond to the genes listed in Table 69. The top of the table states that SEQ ID Nos 2240-2265 (25 Seq ID Nos) corresponds to the listed genes. However, there are only 14 listed genes. Because the GenBank ID do not exist in the GenBank database and the SEQ ID Nos do not correspond to the listed genes, it is unclear what subject matter is claimed and is to be searched.

Response to Arguments

8. The Applicant has supplied amendments to the specification such as the footnote to be added to page 88 of the specification. However, because the SEQ ID Nos do not correspond to the listed genes, the amendments to the specification do not clarify which SEQ ID Nos describe which genes.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 1-28 and 36-38 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims are drawn to a process involving the judicial exception of a computational algorithm. Claims drawn to a judicial exception is non-statutory unless the claims include a practical application of that judicial exception as evidenced by a

physical transformation of the claimed invention, or if the claimed invention produces a useful, tangible and concrete final result. In the instant claims, there is no physical transformation by the claimed invention, thus the Examiner must determine if the instant claims produce a useful, tangible, and concrete final result. See MPEP 2106.

The instant claims do not produce a tangible final result. A tangible final result requirement requires that the claim must set forth a practical application of the mathematical algorithm to produce a real-world result. The instant claims are drawn to a method of identifying a subset of genes within a concordance set and recording the genes. Although the last step records the list of genes, it is unclear if that recording is accessible to a user. In other words the subset of genes may be recorded within a computer and never communicated to the outside world. Thus the instant claims do not require that a tangible result must be produced. This rejection could be overcome by amendment of the claims to identify/recite a concrete result and to recite that the result is outputted to a display or to a user or outputted in a user readable format. However, applicant is reminded that any amendment must be fully supported and enabled by the originally filed disclosure.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Backert et al. (Int. J. Cancer (1999) Volume 82, pages 868-874) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991).

The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data.

Regarding 1, Backert et al. teach using two samples that different with respect to phenotype and determining a reference set of genes (page 869, left column; page 870, paragraph bridging left and right column), identifying a second reference set of expressed genes independent of the first reference set from a third and fourth sample (page 870, right column, second full paragraph; page 871, left column); identifying a concordance set of expressed genes (page 870, right column, bottom full paragraph; page 871, left column). Furthermore, Backert et al. recorded the genes identified in the description of the genes that have lowered expression (page 870, right column, bottom full paragraph).

However, Backert et al. do not teach determining a correlation coefficient that exceeds a predetermined value.

Regarding claim 1, Bertucci et al. teaches determining the correlation coefficient that exceed a predetermine value for correlating genes (page 2987, right column, 2nd full paragraph).

Regarding claims 2-6, Bertucci et al. teach determining a correlation coefficient (page 2987, right column, 2nd full paragraph); logarithmically transforming the

differentials (page 2987, right column, 3rd full paragraph); wherein the correlation coefficient has an absolute value greater than 0.98 (page 2987, right column, 2nd full paragraph).

Regarding claims 8-11, Bertucci et al. teach wherein the gene expression data is cDNA or RNA quantification data (page 870); wherein the sample comprises of a cell line, which is a tumor cell line (page 869, left column, top).

Regarding claims 16-19, Bertucci et al. teach wherein the sample is from a patient, a healthy donor, is a tumor cell, or from the colon (paragraph bridging pages 869-867).

Regarding claim 20, Bertucci et al. teach where the phenotype is selected from lymph node status (page 2983, left column, bottom section).

Regarding claim 21, Bertucci et al. teach where a plurality of independent samples is used for each sample (paragraph bridging page 869-870); and where the differential is an average over the sample (page 870, Table II).

Regarding claim 22, Bertucci et al. teach determining a second correlation coefficient with a positive sign that establishes a positive correlation with a phenotype (page 2983, right column, first full paragraph).

Regarding claim 23, Bertucci et al. teach that ERBB2 had the highest correlation of the genes tested (page 2983, first full paragraph) and since its correlation was the highest its correlation was the most reliable indication of cancer (abstract; page 2985, left column, bottom paragraph – right column, top paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Backert et al. with Bertucci et al. to gain the advantage of determining the reproducibility of experiments. One of the challenges that face gene expression experiments is the precision of the equipment used in those experiments. Given the same experiment, the equipment may produce different results. Given the uncertainty of the equipment as well as the need to compare data from different sources, one of ordinary skill in the art would seek to verify the reproducibility of experiments to ensure that their interpretation of the data is correct. Backert et al. recognized the need to find determine the accuracy of gene expression experiments (page 871, right column, under discussion). Bertucci et al. teaches a method of determining the accuracy of gene expression using a correlation coefficient (page 2987, right column, 2nd full paragraph). Given that Backert et al. recognizes the need for determining the accuracy of a gene expression experiment, and Bertucci et al. provides for such a need, one of ordinary skill in the art would be motivated to combine the methods of Backert et al. and Bertucci et al. to ensure that the gene expression data was accurate.

Response to Arguments

13. The Applicant has responded to this rejection by amending claim 1 to include the limitation of "identifying a second set of expressed genes independent of the first set. . . ." and arguing that Backert et al. and Berucci et al. do not teach identifying a second set of genes that is independent of the first set. The Examiner disagrees. Applicants

appear to be equating independent with different. However, a set that is independent of another set merely means that one set does not control the other set. Although Backert et al. uses the same cell lines, his experiments are conducted independently of the other experiments. In other word, one experiment did not control the results of the other experiment. Thus each experiment created its own reference set that is independent of the other experiments.

Secondly, the Applicant states Backert et al. verifies those 10 alterations through a Northern blot/RT-PCR. While this is true, it is unclear how the Northern blot/RT-PCR experiment is not an independent test with independent results. The results of the Northern blot/RT-PCR experiment did not depend on the results of the cDNA array experiment. In fact, the Northern blot/RT-PCR experiment obtained different results (i.e., a different reference set) and only verified 6 of the 10 gene alterations of the cDNA array experiment (page 870, right column). Thus Backert et al. do teach a concordance set between two independent sets.

The Applicant also questions the Examiner's citation of experiments regarding human tissue. The Examiner was presenting these experiments as an alternative way of interpreting the third and fourth samples. The Applicant states that the human tissue experiments do not produce a second independent reference set because the same 10 alterations were examined. The Examiner disagrees. The results of the human tissue experiment did not depend on the results of the cDNA array experiment. Rather, the human tissue experiment obtained different results (i.e., a different reference set) from

the cDNA array experiment and only identified two genes with altered gene expression.

Because the sets are independent, a concordance set may be found.

Finally, the Applicant states that Bertucci et al. does not disclose two reference sets. However, the Examiner was not relying on Bertucci et al. to disclose two reference sets, but to teach determining the correlation coefficient.

14. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Backert et al. (Int. J. Cancer (1999) Volume 82, pages 868-874) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991) further in view of Young et al. (US #2005/0255588 A1).

The instant claims are drawn to identifying a subset of genes using a correlation coefficient calculated from gene expression data and using samples comprising omnipotent or pluripotent cells.

Backert et al. and Bertucci et al. are applied as above.

However, neither Backert et al. nor Bertucci et al. teach using pluripotent or omnipotent stem cells.

Young et al. teach creating samples of pluripotent or omnipotent stem cells (page 3, paragraph 0019-0020).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the cell lines described in Young et al. with the methods of Backert et al. and Bertucci et al. The motivation to combine Backert et al. with Bertucci et al. is provided above. It is recognized in the art the use of stem cells could potentially provide

many new applications in science and medicine (Young et al., page 3, paragraph 0015-0016). However, it is unclear what genes are expressed to maintain a cell as a stem cell. Thus one of ordinary skill in the art seeking to understand the gene expression of stem cells would be motivated to determine what genes are differentially expressed that correspond to the stem cell phenotype. Backert et al. provide a method of identifying the correct identification of the differences in gene expression between different cell lines (Backert et al., page 873, right column, bottom). Backert et al.'s method could identify the differences in gene expression in a stem cell as compared to other cells. Thus one of ordinary skill in the art seeking to understand the gene expression of stem cells would be motivated to take the sample cell lines disclosed by Young et al. and use those samples in the method provided by Backert et al.

Response to Arguments

15. The Applicant has responded to this rejection by arguing that Backert et al. and Bertucci et al. do not teach all the limitations of claim 1. See above for the Examiner's response.

Conclusion

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00-6:30, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jerry Lin/
Examiner, AU 1631
2/1/2008